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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,509	06/13/2005	Herman Jan Tijimen Coelingh Bennink	0470-045922	1291

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EXAMINER	
JEAN-LOUIS, SAMIRA JM	
ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,509	COELINGH BENNINK ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-32* is/are pending in the application.

4a) Of the above claim(s) *17-27 and 29-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *Sheets (2)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 17-32 are currently pending in the application.

Applicant's amendment of claim 28 and election of Group II (i.e. method of treating vaginal dryness) in the reply filed on 01/22/08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Thus, the requirement is deemed proper and is therefore made FINAL.

Claims 17-27 and 29-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group and species, there being no allowable generic or linking claim.

Objections

The abstract of the disclosure is objected to because it contains legal phraseology such as "comprising" and "selected from the group consisting of" in lines 2 and 12. In addition, the abstract should commence on a separate sheet under the heading "Abstract" (i.e. without any title on the abstract page). Correction is required. See MPEP § 608.01(b).

IDS

The information disclosure statement filed on June 03, 2005 (specifically items WO 00/62753) fails to comply with 37 CFR 1.98(a) (3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but only the information referred to in the abstract therein has been considered. Additionally, U.S. Patent 5,063,507 has not been considered as it relates to a computer database transaction which is non-analogous art.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 28 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating vaginal dryness, does not reasonably provide enablement for a method to prevent vaginal dryness. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Importantly, given that the term "prevention" implies an absolute term, it is

assumed that no known disease can be absolutely prevented at this time. For example, applicant does not reasonably provide enablement for a method to prevent vaginal as vaginal dryness results from menopause due to low estrogen level and menopause is a biological event that cannot be prevented. Additionally, the application does not enable any person skilled in the art to use the invention to prevent vaginal dryness.

The instant claims are drawn to a method of treating or preventing vaginal dryness by applying at least a 5 µg/g of an estrogenic component of a formula and a cosmetically acceptable carrier. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention as claimed.

Attention is directed to *In reWands,* 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to a method of treating or preventing vaginal dryness by applying at least a 5 µg/g of an estrogenic component of a formula and a cosmetically

acceptable carrier. The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites the above fact where vaginal dryness is a symptom of menopause which cannot be prevented.

2. The breadth of the claims

Since the instant specification provides no limiting definition of the term "prevention", the examiner will adopt the broadest reasonable interpretation for same. Webster's Ninth New Collegiate Dictionary defines "prevention" as "to keep from happening or existing", i.e., to completely eradicate.

The claims are thus very broad insofar as they recite the "prevention" of vaginal dryness, i.e., the complete eradication of same. While such "prevention" might theoretically be possible under strictly controlled laboratory conditions, as a practical matter it is nearly impossible to achieve in the "real world" in which patients live.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for a method for preventing vaginal dryness by applying at least a 5 µg/g of an estrogenic component of a formula and a cosmetically acceptable carrier. In fact, applicant only provided guidance for treating vaginal dryness

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed estrogenic compound could be predictably used to prevent vaginal dryness as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation in order to determine if said estrogenic component claimed by applicant can prevent vaginal dryness, with no assurance of success.

Genentech, 108 F.3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, a method for preventing vaginal dryness comprising applying at least a 5 µg/g of an estrogenic component of a formula and a cosmetically acceptable carrier is not considered to be enabled by the instant specification.

The claims are examined herein for a method of treating vaginal dryness.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

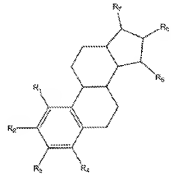
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 28 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As stated by the court in Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886, 1892 (CAFC 2004), regarding the written description requirement:

> The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its functioning of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice.... The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described.

In this instant application, applicant did not specifically describe an estrogenic compound represented by the formula,



with the methyl group missing at the C-18 position. For example, applicant discloses compounds of a formula entailing estrogenic compounds such as estetrol containing a methyl group at the C-18 position (see spec. pg. 3-4) and yet the aforementioned claim discloses a formula without a methyl group at the C-18 position. Consequently, due to this lack of written description, the exact interpretation of the aforementioned formula being claimed by applicant cannot be fully ascertained. However, for the purpose of compact prosecution, Examiner will construe that the stated species set forth in the claim contain a methyl group at the C-18 position.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 28 is rejected under 35 U.S.C. 103 (a) as being unpatentable over Kragie (U.S. 2004/0192598 A1) in view of Willhite et al. (Pharmacotherapy, 2001, Vol. 21, Issue 4, pgs. 464-480).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Kragie teaches the use of compositions that can replace the role of estrogens in the functions of humans (see abstract). Kragie also teaches compositions comprising estrogen function replacement agent (s) (EFR) that can replace the role of estrogens, such as estradiol, in the functions of humans and animals (see pg. 2, paragraph 0013). Examples of such agents include derivatives of estradiol such as estetrol (i.e. a compound of the aforementioned formula which reads on claim 28; see pg. 4, paragraph 0038 and pg. 11, claim 7). The dosage of the EFR is provided for sufficient biological activity for the desired estrogen function at the tissue target and needs to

minimally meet the EC50 value (half maximal efficacy concentration) for the desired estrogen function (see pg. 5, paragraph 0044) and can be administered with a suitable carrier (see pg. 6, paragraph 0051). Of interest, Kragie described the EFR containing compositions as useful for menopause. Kragie further pointed to the current use of EFR as useful in perimenopausal and post-menopausal women for treatment of vaginal atrophy and urogenital atrophy (see pg. 8, paragraph 0073).

Kragie does not specifically teach a method of treating vaginal dryness using at least 5 μg/g of estetrol. However, to one of ordinary skill in the art, it would have been obvious to optimize the appropriate dosage that would produce the desired estrogenic function.

Moreover, it is generally noted that differences in concentration or range do not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Given that applicant did not point out the criticality of specific ranges or percentages of the invention, it is concluded that the normal desire of scientists or artisans to improve upon what is already generally known would provide the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.

Whillhite et al. has been provided to demonstrate that urogenital atrophy is also known as vaginal dryness (see Introduction Section). Consequently, Kragie necessarily meets the limitation of claim 28 .

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious utilize the method of Kragie with a desired amount of estetrol since Kragie teaches the use of estradiol derivatives such as estetrol in amounts that would produce the desired estrogenic function. Given that Kragie teaches the use of ERF agents to treat urogenital atrophy (i.e. vaginal dryness as disclosed by Willhite et al.) and ERF like compounds such as estetrol, one of ordinary skill would have been motivated to utilize estetrol to treat vaginal dryness with the reasonable expectation of providing a method that is efficacious in treating vaginal dryness and efficacious in producing desirable estrogenic function.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 28 is rejected under 35 U.S.C. 103 (a) as being unpatentable over the Abstract of Sitruk-Ware et al. (Shweiz. Rundsch, Med. Praxis, 1997, Vol. 86, No.

33, pg. 1245-1248, already cited by applicant and filed on an IDS 1449 form) in view of Spicer (U.S. 5,211,952) and in further view of Willhite et al. (Pharmacotherapy, 2001, Vol. 21, Issue 4, pgs. 464-480).

The Abstract of Sitruk-Ware et al. teaches that urogenital symptoms is due to low estrogen after menopause. This low estrogen is further taught to lead to vaginal irritation and vaginal dryness. The abstract of Sitruk-Ware et al. further teaches that estrogenic treatment is an efficient way to correct the aforementioned symptoms. Sitruk-Ware further teaches that treatments with low adverse effects and low doses are preferred. Sitruk-Ware et al. further teaches estrogen compounds at low doses such as 7.5 µg/day for prolonged release regimen in the treatment of urogenital atrophy.

The Whillite and Sitruk-Ware et al. references are as discussed above and incorporated by reference herein. However, Sitruk-Ware and Willhite do not address the use of an estrogenic component with the aforementioned formula.

Spicer et al. teaches preparations for use for extended period of time comprising gonadotrpopins (GnRH) and estrogenic compounds (see col. 1, lines 9-11). Spicer et al. further teaches the addition of estrogenic steroids for counteracting the possibility of side effects such as urogenital atrophy which may develop during prolonged therapy including (col. 3, lines 25-46). Estrogenic steroids such as estetrol may be employed in the composition and formulated for vaginal delivery (col. 5, lines 49-53, and 60, and col.

6, line 68). These compositions can further include a carrier vehicle known for controlled release (see col. 7, lines 1-5).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the composition of Spicer et al. in view of their efficacy in combating urogenital atrophy (i.e. vaginal dryness as disclosed by Willhite et al.) in the method of treating urogenital atrophy of Sitruk-Ware et al. Given that Sitruk-Ware et al. teaches a method of treating vaginal dryness or urogenital atrophy, and Spicer et al. teaches the use of estrogenic compound such as estetrol for combating urogenital atrophy, one of ordinary skill would have been motivated to utilize at least 7.5 µg/day of an estrogenic compound to treat vaginal dryness as disclosed by Sitruk-Ware et al. and use estetrol as the preferred compound given the disclosure of Spicer et al. with the expectation of providing a method that is efficacious in counteracting GnRH side effects including treatment of vaginal dryness.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

03/14/2008

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617